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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
NGUYEN, DAVE TRONG

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/22/2002 11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/553,552	Applicant(s) LANGER ET AL.	
	Examiner Dave Nguyen	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,14-32,35,39,41,42 and 44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,14-32,35,39,41,42 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed action* .

Claims 1, 5, 14, 17, 32, 39, 42 have been amended, claims 13, 33, 34, 36-38, 40 and 43 have been canceled by the amendment filed Feb. 20, 2002.

Give that the prior art of record does not teach or suggest the any of species as recited in the presently pending claims, all of the non-elected species have been rejoined for examination and the species restriction of record has been withdrawn by the examiner.

Claims 1-12, 14-32, 35, 39, 41, 42, 45, to which the following grounds of rejection remain applicable, are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12, 14-32, 35, 39, 41, 42, 45 readable on genera of: 1/ a genus of compounds having one or more hydrolyzable functional moieties, wherein the compound must exhibit the endosomolytic activity in response to a change in pH, 2/ a subgenus of 1/ wherein the compounds further have the ability to mask or encapsulate a lytic agent including a solution of ethanol when not present in an endosome, 3/ a subgenus of 1/ wherein the compounds further have one or more ionizable functional moieties, and wherein the hydrolyzable functional moieties and the ionizable functional moieties function as a whole to lyse the endosome; and 4/ a genus of packaging agents that must exhibit the biological activity of complexing directly or indirectly with the compounds of 1/ and of packaging and delivering a desire molecule to the cytoplasm of a cell, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

While the as-filed specification only provides sufficient written description of monomers having one or more hydrolyzable functional moieties or one or more ionizable moieties so as to exhibit a

hydrophobic/hydrophilic transition in response to a change in pH and protonation activity, respectively (page 7 bridging page 8, for example), the as-filed specification does not provide sufficient written description of a representative number of species of polymeric nanoparticles having specific formula or structure **so as to exhibit an endosomolytic activity**. The compounds composed of just ortho-esters, hydrzones, and cis-actonyls do not *per se* exhibit the endosomolytic activity which is the essential feature of the invention, *e.g.,* also see page 6 of Applicant's response. The as-filed specification only provides sufficient description of an endosomolytic lysing polymer comprising an endosomolytic agent and one or more hydrolysable functional moieties selected from the group consisting of ortho-ester, hydrzones, and cys-actonyls, wherein said polymer is capable of effecting the lysis of an endosome in response to a change in pH. A description of other monomers having hydrolyzable moiety of hydrazone or cis-actonyl is not the same as a disclosure of specific formula or structure of polymeric structure that must exhibit the property of being able to complex with a substance to be delivered into a cell, to transfect a cell through the endosome at a size of less than 150 nm, and to exhibit an endosomolytic activity subsequently thereby releasing the substance into the cytoplasm in an intact form and sufficient amount of the substance for any beneficial utility. Furthermore and with respect to the subgenus of 2/, the as-filed specification contemplates on the basis of its written description that the polymeric nanoparticles can be linked structurally to an endosomolytic functional moiety other than those known in the prior art so that the moiety is only active (released, contacted, and disrupting the lipid bilayers of the endosome) when the polymeric nanoparticles undergo a hydrophobic/hydrophilic transition in response to a change in pH, however, the as-filed specification does not provide any substantial and specific description of the formula or structure representing the subgenus of 2/ and/or a representative number of species of endosomolytic functional moieties other than **ethanol** and those known in the prior art and excluded by the as-filed specification, *e.g.,* chloroquine, fusogenic peptides, inactivated adenoviruses and polyethyleneimine (page 7, second paragraph)

With respect to the subgenus of 3/ which is embraced by the genus of 1/, the specification also does not provide sufficient written description of specific structure(s) and formula of polymeric

nanoparticles comprising monomers having one or more hydrolyzable functional moieties which exhibit a hydrophobic/hydrophilic transition in response to a change in pH, and one or more ionizable functional moieties, which moieties must function to increase the hydrophilicity of the polymeric nanoparticle by protonation in the endosome to the extent that the moieties exhibit an endosomolytic activity (page 9 of the specification).

With respect to claims readable on a genus of packaging agents that must exhibit the biological activity of complexing directly or indirectly with the compounds of 1/ and of packaging and delivering a desire molecule to the cytoplasm of a target cell, the as-filed specification only provides sufficient description of packaging agents composed of cationic polymers either copolymerized with the polymeric nanoparticle of 1/ or forming a mixture with the polymeric nanoparticle of 1/.

In view of the reasons set forth in the preceding paragraphs, it is apparent that on the basis of applicant's disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or assays (page 11 of the specification) and/or any other unspecified structure containing unspecified compounds and/or packaging agents that are only described by functional language, wherein the detailed and common structure of the genera of the claimed compounds was not described; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of biochemical or molecular structure(s) of component(s) that are linked structurally in order to exhibit the disclosed biological functions as contemplated by the as-filed specification.

It is not sufficient to support the present claimed invention directed to component(s) with no chemical structure described for the genera of 1/ and/or 2/ and/or 3/ and/or 4/ because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any and/or all other material(s) of compounds other than those known in the prior art, as admitted by the as-filed specification (claim 45) having the biological functions as contemplated by the specification and the claims. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which is not conventional in the art as of

applicants effective filing date. Claiming unspecified molecular structures of material(s) having hydrolyzable functional moieties, masking and/or encapsulating activities, ionizing elements, and/or packaging agents that must possess the biological properties (importing a desire molecule through the endosome to the cytoplasm of a target cell as a result of endosomolysis) as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure structure(s) of material(s) other than , as contemplated and asserted by the as-filed specification to the extent that those polymeric nanoparticles once formed would exhibit the contemplated biological functions (importing and endosomolytic activities), and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification.

Thus, In view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Applicant assert on page 4 of the response that due to the claim amendment, applicant had possession of the claimed invention at the time the invention was made, the comments are not found persuasive because of the reasons set forth in the stated rejection. Note that The as-filed specification only provides sufficient description of an endosomolytic lysing polymer comprising an endosomolytic agent and one or more hydrolysable functional moieties selected from the group consisting of ortho-ester, hydrzones, and cys-actonyls, wherein said polymer is capable of effecting the lysis of an endosome in response to a change in pH.

Claims 1-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for claims limited to:

1) An endosomolytic lysing polymer comprising an endosomolytic agent and one or more hydrolysable functional moieties selected from the group consisting of ortho-ester, hydrzones, and cys-actonyls, wherein said polymer is capable of effecting the lysis of an endosome in response to a change in pH;
2) The polymer of 2/ further comprises a cationic polymer;
3) A cell delivery composition comprising the polymer of 1/ and a compound to be delivered to a cell;
4) A method of employing the lysing polymer of 1/ to lyse an endosome; and
5) A method of delivery a compound to a cell comprising administering the composition of 3/ to a cell.
6) A method for introducing a nucleic acid into a cell or a subcellular component, the method comprising the steps of:

   Providing a biocompatible delivery composition comprising an endosomolytic lysing polymer comprising an endosomolytic agent and one or more hydrolyzable functional moieties selected from the group consisting of ortho-ester, hydrazones, and cys-actonyls, wherein said polymer is capable of effecting the lysis of an endosome in response to a change in pH;

   A nucleic acid; and contacting the composition with cells;

7/ The method of 6), further comprising contacting the composition with cells in the absence of a known endosomal lysing component selected from the group consisting of chloroquine, polyethyleneimine, fusogenic peptides, inactivated adenoviruses and combination thereof, wherein the composition comprises ethanol as the endosomolytic agent.

The specification does not reasonably provide enablement for the presently pending claims encompassing any and/or all structure other than those as indicated in the enabling embodiments, and any other embodiments in the context of artificial virus as claimed in claim 36. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Specifically, since the claimed invention is not supported by a sufficient written description (for possessing of the genus of compounds and/or packaging agents and/or artificial viruses), particularly in view of the reasons set forth above, one skilled in the art would not known how to use and make the claimed invention so that it would operate as intended, *e.g.* functions as a delivery vector to deliver any compound to the cell cytoplasm intact through an endosome of cell targeted for delivery.

To the extent that the claims encompass embodiments that meet the written description from the as-filed specification, the specification coupled with the state of the art of record only provides sufficient guidance and/or factual evidence to enable claims readable on an endosomolytic lysing polymer composed of a poly(ortho-esters) having one or more tertiary amine group, wherein said polymer is capable of effecting the lysis of an endosome in response to a change in pH.

The as-filed specification contemplates that as long as polymeric nanoparticles comprises a hydrolyzable functional moiety, *e.g.,* ortho-ester, hydrazones and cis-actonyls, and/or an ionizable moiety, *e.g.,* N-methacryloyl-L-histidine, the nanoparticles would exhibit the ability to lyse and/or encapsulate and/or mask any endosomolytic agent (ethanol) **so as t lyse an endosome** in response to a change in

pH thereby releasing a desire compound into the cytoplasm of a cell. The as-filed specification further contemplates that any polymeric nanoparticle can be even used to mask and/or encapsulate volatile organic solvent such as ethanol together with a compound including nucleic acid or RNA to delivered to a cell so that ethanol is released only in an endosome of the cell thereby releasing the compound into the cytoplasm in an intact form so as to perform its biological activity. However, no description of formula or structure of those encapsulating polymers or sufficient guidance as to those encapsulating polymers having an intact core of ethanol is provided by the as-filed specification. While the as-filed specification also provides guidance for the making of one exemplified polymeric nanoparticle, *e.g.*, nanoparticles composed of N-[2-methyl-1,3-O-ethoxyethylidine-propanediol]methacrylamide (protected by an orthoester) that is further used to contain DNA molecules. However, no factual evidence is provided to indicate a successful delivery of the DNA molecules into the cytoplasm of a cell through its endosome in intact forms.

The state of the prior art with respect to the art of employing polymeric compounds other than those disclosed in claim 45 (which compounds are also excluded by the as-filed specification) an a cell delivery/endosomolytic vector remains unpredictable at the time the invention was made. While the making of monomers comprising functional hydrolyzable moieties and/or ionizable moieties is conventional in the prior art of record, the issue is whether or not a skilled artisan would have required an undue experimentation to identify and/or make the claimed polymeric nanoparticles that exhibit the ability to import a compound into an endosome and subsequently lyse the endosome thereby releasing the compound into the cytoplasm in an intact form. The state of the prior art exemplified by Hope *et al.* (Molecular Membrane Biology, 15, 1-14, 1998) indicates (page 11, column 1):

"Unfortunately, the role of endosome maturation and fusion with lysosomes in the transfection process is unclear. Some reports demonstrate that lysosomotropic agents such as ammonium chloride, chloroquine and monesin inhibit transfection (Gao and Huang 1995), whereas others show that gene transfer (Zabner *et al.* 1995) and oligonucleotide delivery (Zelphati and Szoka Jr. 1997) are either enhanced or their presence [presence of lysosomotropic agents) makes no difference. Consequently, the

importance of intracellular processing in the release mechanisms remains to be determined".

More specifically as to even the preferred embodiment of the claimed invention wherein a polymer composed poly(ortho esters) comprising any hydrolyzable functional moiety for use as an delivery and endosomolytic vector, Heller *et al.* (J. of Controlled Release, 13, pp. 295-302, 1990) indicates (page 297, column 2):

"In initial studies [3] using a crosslinked poly (ortho ester) system we found that its acid sensitivity was not adequate, but we also found that increasing the polymer hydrophilicity or decreasing crosslink density did increase acid-sensitivity. Unfortunately, this increase was not sufficient to make this system a useful candidate. However, the acid sensitivity of poly(ortho esters) could be significantly increased by the incorporation of tertiary amine groups into the polymer structure".

Thus, Applicant's contemplation that any polymer compound having any hydrolyzable functional moiety and/or ionizable moiety would import any compound to DNA molecules to an intracellular endosome *in vitro* and/or *in vivo* and subsequently lyse the endosome in response to a change in pH thereby releasing the compound into the cytoplasm in an intact form is supported by neither the state of the art of record or the basis of applicant's disclosure. In fact, even with the established studies on the use of cationic polymers including lipid polymer/DNA complexes to protect, condense, import DNA into an intracellular endosome and mediate DNA escape from the endosome, Pouton CS: Biological Barriers to gene Transfer. In advanced gene Delivery: From concepts to Pharmaceutical Products, Rollan A, Harwood Press, 1998, pages 65-102, provides factual evidence on page 87 bridging page 88 indicating while polycationic lipid polymers have been used to condense, protect and mediate DNA molecule's transport into an endosome, the polymer was not able to uncouple the DNA in the cytoplasm after endosomolysis, that no gene expression was observed due to the inability of the polymer to uncouple the DNA in the cytoplasm and nucleus, and that control of uncoupling of DNA and condensing agent is a critical process in gene delivery. Pouton CS further indicates on page 88 that "the condensing agent must form a strong enough complex to protect DNA during transport, but must be able to dissociate at the appropriate time, or in the appropriate environment".

In addition, Pouton further indicates on page 88 that understanding and developments of non-viral vectors that can immitate the ability of viruses to exhibit both the ability to mediate endosomal escape and successfully express a gene in the cytoplasm/nucleus remains to be established, and that "cytoplasmic transport is a limitation in non-viral gene delivery but these issues have not been resolved adequately as yet". Furthermore, even two years after the effective filing date of the claimed invention, Hwang *et al.* (Current Opinion in Molecular Therapeutics, 3, 2, pp. 183-191, 2001) teaches:

"A conclusion that can be drawn from polymer-DNA condensation studies is that the size, morphology and charge of the polyplexes [polymer/DNA complexes] generally do no predict the *in vitro* or *in vivo* transfection efficiencies" (page 184, column 1, last paragraph); and

"Thus, the ability to bind and condense DNA into compact structures appears to be a necessary but not sufficient condition to provide efficient gene delivery. Issues such as polymer solubilities, pKA values of the polymer charged groups and DNA binding constants of the polymers must also influence delivery efficiencies. Thus, further work on more detailed physicochemical characterizations are merited (page 184, column 1, last paragraph).

Thus, the as-filed specification does not provide sufficient guidance and/or evidence showing as to how nanoparticle/compound or nanoparticle/DNA complexes that must be of appropriate size to fit inside an endosome (150 nm or less) will be able to lyse the endosome at appropriate time and subsequently uncouple the compound or DNA in uncondensed and intact form for their biological activity, let alone the problem of *in vivo* transient gene expression by using non-viral vectors, as indicated by the art of record, that does not result into any beneficial effect of the DNA in any of the well-known or disclosed therapeutic utilities as contemplated by the as-filed specification.

At best, the as-filed specification and the state of the prior art of record only provides a reasonable enablement for claims directed to:

7) An endosomolytic lysing polymer comprising an endosomolytic agent and one or more hydrolysable functional moieties selected from the group consisting of ortho-ester, hydrzones,

and cys-actonyls, wherein said polymer is capable of effecting the lysis of an endosome in response to a change in pH;

8) The polymer of 2/ further comprises a cationic polymer;

9) A cell delivery composition comprising the polymer of 1/ and a compound to be delivered to a cell;

10) A method of employing the lysing polymer of 1/ to lyse an endosome; and

11) A method of delivery a compound to a cell comprising administering the composition of 3/ to a cell.

12) A method for introducing a nucleic acid into a cell or a subcellular component, the method comprising the steps of:

Providing a biocompatible delivery composition comprising an endosomolytic lysing polymer comprising an endosomolytic agent and one or more hydrolyzable functional moieties selected from the group consisting of ortho-ester, hydrazones, and cys-actonyls, wherein said polymer is capable of effecting the lysis of an endosome in response to a change in pH;

A nucleic acid; and contacting the composition with cells;

7/ The method of 6), further comprising contacting the composition with cells in the absence of a known endosomal lysing component selected from the group consisting of chloroquine, polyethyleneimine, fusogenic peptides, inactivated adenoviruses and combination thereof, wherein the composition comprises ethanol as the endosomolytic agent;

particularly in view of the disclosure of the as-filed specification and the disclosures of the state of the art of record.

Applicants assert that due to the examples starting on page 20 of the specification which teach that nucleic acids can be encapsulated in the claimed endosomal lysing agents, and given that other hydrolyzable linkages such as hydrazones and actonyls would function as well, the comments are not found persuasive because of the reasons set forth in the stated rejection. Note that while the making of

monomers comprising functional hydrolyzable moieties and/or ionizable moieties is conventional in the prior art of record, the issue is whether or not a skilled artisan would have required an undue experimentation to identify and/or make the claimed polymeric nanoparticles that exhibit the ability to import a compound into an endosome and subsequently lyse the endosome thereby releasing the compound into the cytoplasm in an intact form. The essential feature of the invention is claiming a product that can lyses an endosome in response to pH, the making of the monomers composed of hydrazones, and cys-actonyls is not the same as claiming a composition that entraps, delivers DNA, lyses an endosome so as to release the DNA into the cytoplasm. The essential feature is the requirement of a polymer delivery carrier that contains one or more hydrolyzable functional moieties selected from the group consisting of ortho-ester, hydrazones, and cys-actonyls, and an endosomolytic agent which includes known endosomolytic agents and ethanol. As such, the claims remain properly rejected under 35 USC 112, first paragraph, particularly in view of the reasons set forth above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32 is indefinite because it is not apparent as to which of endosomolytic agents of claim 1 or 5 "an endosomolytic agent of claim 1or 5" refers to. A change to -- the endosomolytic agent of claim 1 or 5 -- would obviate the rejection.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst Dianiece Jacobs, whose telephone number is **(703) 305-3388.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Dave Nguyen* whose telephone number is **(703) 305-2024**.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Deborah Reynolds*, may be reached at **(703) 305-4051.**

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is **(703) 305-7401**.

Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is **(703) 308-0196**.

Dave Nguyen
Primary Examiner
Art Unit: 1632

DAVE T. NGUYEN
PRIMARY EXAMINER